REMARKS

Applicants acknowledge the current status of the claims, as reported in Office Action dated 01 February 2006. Claims 4-8, 11-88 and 96-104 are pending; claims 5-8, 11, and 32-88 are withdrawn from consideration; claims 4, 12-31 are allowed; and claims 96-104 are rejected.

Applicants thank the Examiner for the courtesy of Examiner's interview, conducted on 31 July 2006, to discuss the bases of the outstanding rejections to Applicants' application. This interview forms the basis for the present remarks.

Reconsideration and allowance of the pending claims in light of the following remarks are respectfully requested.

Withdrawal of claim rejections:

Applicants acknowledge Examiner's withdrawal of rejection of claims 12-31 under 35 USC §103(a) as being unpatentable over Luger et al. in view of references disclosing specific methods for generating antibodies, and, the rejection of claims 12 and 31 under 35 USC § 112, first paragraph, as lacking enablement commensurate with the scope of the claims, in view of arguments presented by Applicants' in paper filed on 11/9/2005.

Rejections under 35 USC §103(a)

In the Office Action, at page 2, paragraph 4, claims 96-104 are rejected under 35 USC §103(a) as being unpatentable over Luger et. al., Immunobiology, 1986, vol. 172, pp. 346-356 in view of Schmidt et. Al., (EP0218531) and Berg (US Patent 5622701). The Examiner asserts that it would be obvious to one skilled in the art to combine the teachings of Luger et. al., with those of Schmidt et.al. and Berg to produce antibodies capable of binding IL-1a and IL-1b and capable of binding the antigen comprising an amino acid sequence TKGGQDITDFQILENQ (SEQ ID NO. 3). Further, the Examiner asserts that human, chimeric, CDR grafted, and humanized antibodies capable of binding IL-1a and IL-1b and capable of binding the antigen comprising an amino acid sequence TKGGQDITDFQILENQ (SEQ ID NO. 3) would also be obvious to one skilled in the art for the same reasons. Applicants respectfully disagree.

BASIC REQUIREMENTS OF A *PRIMA FACIE* CASE OF OBVIOUSNESS

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.
>
> MPEP §2143

It is well recognized that:

> Hindsight reconstruction of a claimed invention, absent a teaching or suggestion in the art is impermissible.
>
> MPEP §2142

Claim 96 is directed to a dual-specificity antibody, or antigen binding portion thereof to IL-1α and IL-1β wherein the antibody or antigen binding portion is capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ (SEQ ID NO: 3). Claims 97-104 recite specific aspects of Applicants' invention wherein Applicants' dual-specificity antibody is a fully human (claim 98), chimeric (claim 99), CDR grafted (claim 101) or humanized (claim 104) antibody.

Luger et al. teach a fully mouse monoclonal antibody which reacts with IL-1α and IL-1β. The Examiner acknowledges that Luger et al. do not teach antibodies that are capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

Schmidt et al. disclose specific peptides derived from IL-1 (IL-1β) and antibodies to those peptides. Specifically, Schmidt et al. disclose an antibody to the amino acid sequence THR LYS GLY GLY GLN ASP ILE THR ASP PHE THR (TKGGQDITDFT) (Claim 1, page 11, line 2). Schmidt et al. do not teach or suggest an antibody or antigen binding portion capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

Berg discloses monoclonal antibodies capable of binding P-Selectin and E-Selectin. Further Berg discloses human, CDR grafted and humanized antibodies capable of binding P-Selectin and E-Selectin. Berg does not teach or suggests an antibody, or antigen binding portion capable of binding IL-1α and IL-1β, and/or antibodies capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. In addition, Berg does not teach or suggest chimeric, humanized or human dual-specificity antibodies to IL-1α and IL-1β capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

The Examiner asserts that one of ordinary skill in the art would have been reasonably expected to combine the teaching of Luger et al. with those of Schmidt et al. and Berg to produce dual specificity antibodies to IL-1α and IL-1β capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. The Examiner further asserts that one of ordinary skill in the art would be able to produce chimeric, humanized or human dual specificity antibodies to IL-1α and IL-1β capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. Neither Luger et al., Schmidt or Berg, either singularly or in combination, teach or suggest dual specificity antibodies to IL-1α and IL-1β capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ.

Applicants' claimed antibody is a dual specificity antibody to IL-1α and IL-1β , wherein the antibody is capable of binding the antigen with amino acid sequence TKGGQDITDFQILENQ. Specific aspects of the invention are directed to human, chimeric, CDR grafted or humanized dual specificity antibodies capable of binding amino acid sequence TKGGQDITDFQILENQ. The antigen sequence is a hybrid peptide generated by splicing together TKGGQDITDF from IL-1β with ITDFQILENQ from IL-1α. In Examples 3 and 4 on pages 48-50, Applicants disclose how to generate the hybrid peptide antigen TKGGQDITDFQILENQ, and how to make antibodies capable of binding the antigen, and capable of binding IL-1α and IL-1β.

Schmidt et al. disclose various peptides derived from IL-1β, including TKGGQDITDFT, and antibodies capable of binding those peptides. Examiner asserts the antibody to peptide disclosed in Schmidt et al. would bind the antigen disclosed in Applicants' disclosure because 10 of the 16 amino acids are identical, i.e TKGGQDITDFT vs TKGGQDITDFQILENQ. Applicants respectfully disagree. Applicants' peptide is a hybrid peptide as described above. A priori, there is no reason to believe that antibodies to the peptide TKGGQDITDFT disclosed in Schmidt et al., will bind the antigen TKGGQDITDFQILENQ disclosed by Applicants. Furthermore, the antibodies to peptide TKGGQDITDFT derived from IL-1β, bind IL-1β. Schmidt et al do not teach or suggest antibodies to IL-1α nor do they teach or suggest dual specificity antibodies to IL-1α and IL-1β. Schmidt et al do not even mention IL-1α. Therefore, the assertion that antibodies disclosed by Schmidt et al., would bind the antigen disclosed by Applicants is mere conjecture.

Berg discloses monoclonal antibodies capable of binding P-Selectin and E-Selectin. Further Berg discloses human, CDR grafted and humanized antibodies capable of binding P-Selectin and E-Selectin. Berg does not teach or suggest an antibody, or antigen binding portion capable of binding IL-1α and IL-1β, and/or antibodies capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. In addition, Berg does not teach or suggest chimeric, humanized or human

dual-specificity antibodies to IL-1α and IL-1β capable of binding an antigen comprising the amino acid sequence TKGGQDITDFQILENQ. In fact, Berg does not even mention IL-1α or IL-1β, or antibodies to IL-1α and IL-1β.

The Examiner has used Applicants' disclosure as a template to search and reconstruct Applicants' invention. In one aspect, the Examiner has cited Luger et al. as disclosing a fully mouse monoclonal antibody that binds IL-1α and IL-1β. In a second aspect, the Examiner has searched for and cited Schmidt as disclosing antibodies to a peptide that shares partial identity with the antigen disclosed by Applicants. In a third aspect, the Examiner has cited Berg as disclosing antibodies capable of binding P-Selectin and E-Selectin. Luger et al. do not teach or suggest dual specific antibodies capable of binding the antigen TKGGQDITDFQILENQ. Schmidt does not teach or suggest the generation of dual-specificity antibodies. Further, Schmidt does not teach or suggest antibodies to a hybrid peptide such as the one disclosed by Applicants. Finally, Schmidt does not even mention IL-1α. Berg does not even mention IL-1α or IL-1β, or antibodies to IL-1α and IL-1β. The combination of the cited art is made only by the Examiner, upon guidance, direction, and motivation to do so by Applicants' present invention. This is hindsight reconstruction and is impermissible as a basis for rejection under 35 USC §103.

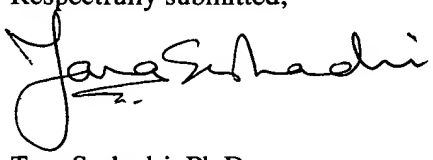
Applicants assert there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings (required as the first criterion to establish a *prima facie* case of obviousness) to create a hybrid peptide with sequences from IL-1α and IL-1β to generate dual specificity antibodies to IL-1α and IL-1β, let alone a human or chimeric dual-specificity antibody to IL-1α and IL-1β capable of binding a specific antigen peptide. Instead, the Examiner has employed impermissible hindsight to fabricate a case of obviousness.

Because the cited art fails to satisfy the criteria necessary to establish or to sustain rejection of claims 96-104 as obvious under 35 USC §103(a), and in view of the foregoing remarks, Applicants respectfully request withdrawal of the rejection of claims 96-104 under 35 USC §103(a).

Conclusion

In view of the foregoing remarks, Applicants believe that all objections and rejections set forth in the Office Action of 01 February 2006 have been avoided or overcome, and consequently the application is in condition for allowance. Reconsideration and removal of the rejections, and allowance of the pending amended claims are, therefore, respectfully requested.

Respectfully submitted,



Tara Seshadri, Ph.D.
Registration No. 48,591
Agent for Applicants